

Claims

- 5 1. An isolated polypeptide comprising one or more of the amino acid motifs selected from the group consisting of a sequence with at least 80% identity to any of
- (a) P-L-X-D-X(35,75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T
- 10 (b) C-X-D-X(3)-S-G-H-T
- (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H.
- 15 2. A polypeptide according to claim 1 that is derived from the group consisting of *Animalia*, *Alveolata* and *Kinetoplastida*.
3. A polypeptide according to claim 1 or 2 selected from the group comprising any of the SEQ ID No. 1 - 11 or at least 70% similarity thereto.
- 20 4. A polypeptide according to claim 1 or 2 comprising an amino acid sequence with at least 70 % similarity to any of the SEQ ID No. 12 - 22.
- 25 5. A polypeptide according to any one of the previous claims comprising an amino acid sequence with at least 20 % identity to any of the SEQ ID No. 12 - 22.
- 30 6. A polypeptide according to claim 5 comprising an amino acid sequence with at least 30 % identity to SEQ ID No. 12.

7. A polypeptide according to claim 5 comprising an amino acid sequence with at least 40 % identity to any of the SEQ ID No. 19 - 21.
- 5
8. A polypeptide according to any one of the claims 1 - 3 comprising an amino acid sequence with at least 22 % identity to SEQ ID No. 22.
- 10 9. A polypeptide according to any one of the claims 1 - 6 with sphingomyelin synthase activity.
- 15 10. A polypeptide according to any one of the claims 1 - 5 and 7 with ethanolamine phosphorylceramide synthase activity.
- 20 11. A polypeptide according to any one of the claims 1 - 5 and 8 with one or more of the activities selected from the group consisting of phosphatidylcholine:glycoprotein cholinephosphotransferase and phosphatidylcholine:glycolipid cholinephosphotransferase.
- 25 12. A nucleotide sequence selected from the group consisting of a nucleotide sequence coding for any of the amino acid sequences as described in claim 9 and an anti sense nucleotide sequence that is complementary thereto.
- 30 13. A nucleotide sequence selected from the group consisting of a nucleotide sequence coding for any of the amino acid sequences as described in claim 10 and an anti sense nucleotide sequence that is complementary thereto.
14. A nucleotide sequence selected from the group consisting of a nucleotide

sequence coding for any of the amino acid sequences as described in claim 11 and an anti sense nucleotide sequence that is complementary thereto.

15. A plasmid comprising any of the nucleotide sequences described in any
5 of the
claims 12, 13 or 14.

16. A vector comprising any of the nucleotide sequences described in any of
the claims 12, 13 or 14.

10 17. A (micro)organism or cell line in which any of the nucleotide sequences
described in claim 12 was introduced.

18. A (micro)organism or cell line in which any of the nucleotide sequences
15 described in claim 13 was introduced.

19. A (micro)organism or cell line in which any of the nucleotide sequences
described in claim 14 was introduced.

20 20. A process for producing sphingomyelin synthase comprising the
expression of
any one of the nucleotide sequences described in claim 12 in a (micro)organism
or cell line of claim 17 and the isolation of sphingomyelin synthase.

25 21. A process for producing sphingomyelin comprising the expression of the
nucleotide sequences described in claim 12 in a (micro)organism or cell of claim
17 and the isolation of sphingomyelin.

22. Use of one of more of the nucleotide sequences of claim 12 to influence
30 the reaction



in vivo or in vitro.

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23. Use of one or more of the nucleotide sequences of claim 12 to identify or develop compounds influencing the reaction

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in vivo or in vitro.

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24. A process for producing ethanolamine phosphorylceramide synthase comprising the expression of any one of the nucleotide sequences described in claim 13 in a (micro)organism or cell line of claim 18 and the isolation of ethanolamine phosphorylceramide synthase.

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25. A process for producing ethanolamine phosphorylceramide comprising the

expression of the nucleotide sequences described in claim 13 in a (micro)organism or cell line of claim 18 and the isolation of ethanolamine

25

phosphorylceramide.

26. Use of any one of the nucleotide sequences of claim 13 to influence the reaction

5 CER + PE \leftrightarrow EPC + DAG

in vivo or in vitro.

27. Use of any one of the nucleotide sequences of claim 13 to identify or
10 develop compounds influencing the reaction

CER + PE \leftrightarrow EPC + DAG

15 *in vivo or in vitro.*

28. The application of the compounds of claim 23 or 27 in medical use.

29. The application of the compounds of claim 28 for the manufacture
20 of medicaments treating a disease selected from the group consisting of cancer, metabolic diseases and diseases caused by parasites.

30. A process for producing phosphatidyl:glycoprotein
cholinephosphotransferase or phosphatidyl:glycolipid
25 cholinephosphotransferase comprising the expression of any one of the corresponding nucleotide sequences described in claim 14 in a (micro)organism or a cell line of claim 19 and the isolation of phosphatidyl:glycoprotein
cholinephosphotransferase or phosphatidyl:glycolipid
cholinephosphotransferase.
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31. A process for producing phosphorylcholine-substituted glycoprotein or

phosphorylcholine-substituted glycolipid comprising the expression of the corresponding nucleotide sequences described in claim 14 in a (micro)organism or cell of claim 19 and the isolation of phosphorylcholine-substituted glycoprotein or

5 phosphorylcholine-substituted glycolipid .

32. Use of one of more of the nucleotide sequences of claim 14 to influence the reaction

10 glyco lipid/protein + PC \leftrightarrow PC-substituted glyco lipid/protein + DAG

in vivo or *in vitro*.

33. Use of one of more of the nucleotide sequences of claim 14 to identify or
15 develop compounds influencing the reaction

glyco lipid/protein + PC \leftrightarrow PC-substituted glyco lipid/protein + DAG

in vivo or *in vitro*.

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34. The application of the compounds of claim 33 in medical use.

35. The application of the compounds of claim 34 for the manufacture of a medicament treating a disease caused by parasitic nematodes.

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36. A process to isolate candidates for functional genes of a previously unidentified enzyme with known activity from a huge database by combining at least four characteristics based on data from bio-informatics and from biochemistry, viz.

- presence of a sequence motif shared with previously identified enzymes having a related function
- biochemical function of the gene should be unknown until now
- no structural homologues in an organism that does not contain the enzyme
- 5 – ability to mediate a reaction catalysed by the unidentified enzyme upon its heterologous expression in an organism or cell lacking said enzyme activity.

37. A process to isolate candidates for functional genes according to claim 36 characterized by also considering the presence or non-presence of
10 transmembrane domains depending on the working mechanism of the enzyme in relation to the membrane.

38. A method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, said activity comprising
15 an activity of an enzyme of the group of enzymes identified as sphingomyelin synthases, ethanolamine phosphorylceramide synthases, phosphatidylcholine:glycoprotein cholinephosphotransferase and phosphatidylcholine:glycolipid cholinephosphotransferase, said method comprising providing said cell with a nucleic acid encoding a polypeptide
20 according to any one of claims 1-11, contacting said cell with said compound and determining whether said enzymatic activity is modulated.

39. A method according to claim 38 wherein said cell is deficient in sphingomyelin synthase activity.
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40. A method according to claim 38 or claim 39, wherein said cell is a cell of a eukaryotic micro-organism.

41. A method according to claim 40, wherein said cell is yeast cell.
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42. A method according to any one of claims 38-41, wherein said polypeptide comprises a sequence as depicted in figure 8 or a functional part, derivative and/or homologue thereof.

5 43. A method according to claim 42, wherein said polypeptide comprises a sequence as depicted in figure 8A or a functional part, derivative and/or homologue thereof.

44. A method according to any one of claims 38-43, wherein said
10 polypeptide is derived from a plasmodium.

45. A method according to claim 44, wherein said plasmodium sequence is a sequence as depicted in figure 8B or a functional part, derivative and/or homologue thereof.

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46. A method according to any one of claims 38-45, wherein said compound comprises RNA.

47. Use of a nucleic acid encoding a polypeptide according to any one of
20 claims 1-11, as a probe.

48. Use of an oligonucleotide specific for a nucleic acid sequence encoding a polypeptide as depicted in figure 8 or a functional part, derivative and/or homologue thereof, for detecting said sequence.

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49. Use according to claim 47 or claim 48, for assessing whether a cell comprises sphingomyelin synthase activity.

50. Use of an inhibitor of a sphingomyelin synthase according to any one
30 of claims 1-11, as a cell death promoter.

51. Use according to claim 50, wherein said cell is a cell of a parasite.

52. Use according to claim 50, wherein said cell is a human cell,
5 preferably a tumor cell.

53. Use of a nucleic acid according to any one of claims 12-14, preferably
comprising a nucleic acid sequence encoding a polypeptide as depicted in figure
8 or a functional part, derivative and/or homologue thereof for enhancing cell
10 survival and/or cell growth.

54. A method for at least in part improving the yield of an secretion
product of a cell comprising providing said cell with a polypeptide according to
any one of claims 1-11, or a nucleic acid according to any one of claims 12-14,
15 preferably comprising a nucleic acid sequence encoding a polypeptide as
depicted in figure 8 or a functional part, derivative and/or homologue thereof.

55. A method according to claim 54, wherein said cell is a cell of a
eukaryotic micro-organism.

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56. A method according to any one of claims 38-46, further comprising
providing said cell or a fraction thereof with a labelled substrate for said
sphingomyelin synthase.

25 57. A method according to claim 56, further comprising harvesting
sphingolipid from said cell or said fraction and detecting labelled sphingolipid.

58. A method according to claim 56 or 57, further comprising detecting
said labelled sphingolipid using (thin layer) chromatography or mass
30 spectrometry.

59. A method for targeting a first polypeptide according to any one of claims 1-11 to a different cellular compartment comprising providing a cytosolic part of said first polypeptide with a cellular compartment localization
5 signal of a cytosolic part of a second polypeptide according to any one of claims 1-11, wherein said first and said second polypeptide, when unmodified, reside in different cellular compartments.

60. A method according to claim 59, wherein said cytosolic part of said
10 first polypeptide comprises the C-terminal end of said polypeptide.

61. A method according to claim 59 or claim 60, wherein said cytosolic part of said second polypeptide comprises the C-terminal end of said polypeptide.
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62. A method according to any one of claims 59-61, wherein said cellular compartments comprises the plasma membrane, the endosomal compartment, the Golgi, the endoplasmatic reticulum or a combination thereof.

20 63. A method according to any one of claims 59-62, wherein said cellular compartment localization signal of said second polypeptide replace the C-terminal cytosolic part of said first polypeptide.